stimulate both physician and patient to be more diligent in their preventive regimen. Prevention is certainly better than cure, because no cure for established diabetic nephropathy is in sight.

ZENO L. CHARLES-MARCEL, MD
LAWRENCE K. LOO, MD
Loma Linda, California

REFERENCES

Cowie CE, Port FK, Wolfe RA, Savage PJ, Moll PP, Hawthorne VM: Disparities in incidence of diabetic end-stage renal disease according to race and type of diabetes. N Engl J Med 1989; 321:1074-1079

Kirkpatrick WG: Can the rate of progression of chronic renal failure be altered? Am J Med Sci 1990; 300:396-401

Reddi AS, Camerini-Davalos RA: Diabetic nephropathy: An update. Arch Intern Med 1990; 150:31-43

Sirmon MD: Renal disease in noninsulin-dependent diabetes mellitus. Am J Med Sci 1990; 300:388-395

Treatment of Chronic Hepatitis C With Recombinant Interferon Alfa

NATURAL ALPHA INTERFERONS are host-derived proteins produced mainly by monocytes and B lymphocytes in response to viral and other stimuli. Because of its antiviral, antiproliferative, and immunomodulatory effects, interferon (IFN) has been used in the treatment of hairy cell leukemia, condylomata acuminata, and Kaposi's sarcoma associated with the acquired immunodeficiency syndrome. Advances in recombinant DNA technology have allowed the production of interferon alfa (IFN-α) in large quantities for clinical use. The Food and Drug Administration has recently added chronic non-A, non-B hepatitis (hepatitis C) to the list of approved indications for treatment with recombinant IFN-α2b.

Hepatitis C is responsible for more than 90% of cases of post-transfusional hepatitis and nearly half of the cases of sporadic hepatitis. About half of the cases of acute hepatitis C will lead to chronic hepatitis, and cirrhosis will develop in 20% of this group. In randomized, controlled clinical trials, 50% of patients with parenterally acquired chronic hepatitis C showed substantial improvement in serum alanine aminotransferase (ALT) levels when recombinant IFN-α2b was administered subcutaneously at a dose of 3 million international units three times a week for six months. This compared favorably with the 5% to 10% per year spontaneous remission rate in untreated patients. Of those responding to IFN-α2b treatment, 70% achieved reductions of ALT to normal levels. Relapse rates approached 50% within six months after the completion of therapy regardless of the dosage used. Retreatment with the initial dose regimen achieved a prompt remission in most patients. Transient elevations of serum ALT levels may occur in some patients after therapy is discontinued, but this by itself is not considered an indication for retreatment. Improvement determined histologically, primarily regression of lobular and periportal inflammation, was also observed in some patients. The presence of the neutralizing antibody to IFN, detected in the serum of some treated patients, did not have a demonstrable effect on the course of the disease or the response to therapy in the short term.

The most frequent side effects of IFN-α2b therapy are flulike symptoms (myalgia, headache, fever) that typically resolve after the first few doses. Other adverse reactions include diarrhea, alopecia, rash, altered mental state, depression, cytopenia, and deranged thyroid function. Reducing the dose temporarily usually ameliorates these symptoms. Current criteria for exclusion from IFN-α2b therapy include decompensated liver disease, cytopenia, other (nonviral) causes of liver disease, serious concurrent medical illness, pregnancy, the presence of antibodies to the human immunodeficiency virus, a previous organ transplant, renal failure, a history of neuropsychiatric problems, autoimmune disorders, and preexisting thyroid abnormalities if thyroid function cannot be maintained in the normal range by medication.

The effect of IFN-α2b therapy on viral replication, infectivity, and the long-term natural history of chronic hepatitis is not known. Current studies will show if higher doses or a longer duration of treatment with IFN-α2b will increase the frequency and duration of remission.

YANG K. CHEN, MD
K. BALA, MD
Loma Linda, California

REFERENCES

Alter MJ, Sampliner RE: Hepatitis C: And miles to go before we sleep. N Engl J Med 1989; 321:1538-1540

Davis GL, Balart LA, Schiff ER, et al: Treatment of chronic hepatitis C with recombinant interferon alfa—A multicenter randomized, controlled trial. N Engl J Med 1989; 321:1501-1506

DiBisceglie AM, Martin P, Kassianides C, et al: Recombinant interferon alfa therapy for chronic hepatitis C. N Engl J Med 1989; 321:1506-1510

Transesophageal Echocardiography

TRANSESOPHAGEAL ECHOCARDIOGRAPHY (TEE) has become an accepted clinical procedure and is considered a logical extension of a complete echocardiographic examination in selected patients. Access to the heart in almost all patients, safety, patient tolerance, and predictably high-quality images have fostered a wide application. Transesophageal echocardiography allows the evaluation of cardiac, valvular, and vascular structures and function in a relatively noninvasive manner. Imaging of the heart through the esophagus provides an unobstructed view of cardiac structures and the great vessels and allows the use of higher frequency transducers, which results in better image quality.

Transesophageal echocardiography examinations are done with an ultrasound transducer mounted at the tip of a modified gastroscope. It can be done in an echocardiography laboratory, in an emergency department, on regular wards, in intensive care units, and in an operating room. In conscious patients, the fasting time before the TEE study should be at least three to six hours. Endocarditis prophylaxis is applied to high-risk patients, especially those with prosthetic valves. Anticoagulation is no longer a contraindication. Patients are generally premedicated, especially those who are apprehensive. A regimen used in our laboratory is 1 to 2 mg of midazolam hydrochloride given intravenously. The posterior pharynx of each patient is anesthetized topically with a 14% benzocaine spray before the procedure.

Conventional transesophageal endoscopes allow imaging in the horizontal plane. Specific limitations of horizontal imaging include difficulty in visualizing extreme anterior and posterior structures and an inability to depict contiguous long-axis or off-axis spatial relationships. Because the heart is a complex organ with three-dimensional relationships and interrelated structures, the ideal tomographic imaging technology should delineate all three anatomic planes. Biplanar imaging has recently become available, adding an orthogonal longitudinal plane and thus enhancing the diagnostic poten-

tial of this technique. Biplanar imaging has now become the method of choice for completely delineating cardiovascular anatomy. The combination of these two planes is superior to either one plane in determining cardiac disease. Specific diagnostic areas of interest include native and prosthetic valves; tumors, thrombi, and vegetations; congenital cardiac defects; aortic aneurysm and dissection; and determining the source of embolism. Complete TEE evaluation of the aorta using a biplanar probe and pulsed Doppler and color flow imaging can diagnose the presence, extent, and type of aortic dissection in virtually every case, and results are comparable to those of computed tomographic scans and magnetic resonance imaging. The advantage of TEE over those techniques is that it can be done at the bedside and in a relatively short time. In addition, TEE can be used intraoperatively and has proved to be of considerable value in assessing the adequacy of a cardiac operation (such as mitral valve repair).

In most cases, TEE is best used as an adjunct to the standard transthoracic, two-dimensional, echo-Doppler examination. Although the clinical indications are rapidly evolving, this technique provides a higher diagnostic yield in patients with suspected endocarditis, prosthetic valve dysfunction, intracardiac thrombi and masses, and aortic dissection.

TAHIR TAK, MD, PhD
P. ANTHONY N. CHANDRARATNA, MD, MRCP
Los Angeles, California

REFERENCES

Daniel WG, Erbel R, Kasper W, et al: Safety of transesophageal echocardiography: A multicenter survey of 10,419 examinations. Circulation 1991; 83:817-821

Geibel A, Kasper W, Behroz A, Przewolka U, Meinertz T, Just H: Risk of transesophageal echocardiography in awake patients with cardiac disease. Am J Cardiol 1988; 62:337-339

Seward JB, Khandheria BK, Edwards WD, Oh JK, Freeman WK, Tajik AJ: Biplanar transesophageal echocardiography: Anatomic correlations, image orientation, and clinical applications. Mayo Clin Proc 1990; 65:1193-1213

Seward JB, Khandheria BK, Oh JK, et al: Transesophageal echocardiography: Technique, anatomic correlations, implementation, and clinical applications. Mayo Clin Proc 1988; 63:649-680

Advance Medical Directives

FOLLOWING THE NATIONAL media attention to the Karen Ann Quinlan case, on January 1, 1977, California's Natural Death Act became the nation's first living will statute. More than 40 states have now enacted similar statutes. More than a decade later, despite widespread public endorsement, less than 10% of Americans have actually made a living will. Recent judiciary and congressional actions, however, should prompt physicians and patients to focus even more on implementing and documenting advance medical directives.

After the highly publicized Nancy Cruzan case, on June 25, 1990, the United States Supreme Court issued its first decision about the "right to die." The Court upheld that the state of Missouri could require "clear and convincing" evidence of Cruzan's wishes before allowing surrogates to authorize the termination of life-sustaining treatment. The continuation of tube feedings for a person in a persistent vegetative state was enforced, even though Nancy Cruzan's earlier statements suggested she would not want such feedings, her family believed she would not want them, and the Supreme Court acknowledged her parents' motives were loving and caring. Thus, the Supreme Court ruling rejected the traditional medical practice of allowing families to make decisions for incompetent patients.

In 1990, Congress passed the Patient Self-determination Act, which took effect on December 1, 1991. Under the law, hospitals, nursing homes, and health maintenance organizations that participate in the Medicaid and Medicare programs must, at the time of admission, provide patients with written information about state laws governing patients' rights to accept or refuse medical treatment and to formulate an advance medical directive. The written policies of the individual hospital or nursing home regarding the implementation of these rights and written documentation whether or not a patient has executed an advance medical directive must also be provided.

Faced with the implications of the Cruzan decision, physicians and patients must act now to avoid situations in which the law may impose restrictions on surrogate decision making. Advance directives, such as a living will, the natural death act, and a durable power of attorney for health care, allow patients to indicate treatments they might wish to have and to designate a surrogate in case they were to become incompetent. It is difficult for a living will to specify all possible treatments for a given circumstance, but a health care proxy allows for greater latitude in future decision making.

While the Patient Self-determination Act may force hospitals and physicians to address this issue with each patient on hospital admission, a better time to start considering this subject would be in the outpatient setting. There, without the distractions of an acute medical illness and allowing sufficient time for discussion and clarification between physicians and patients, along with any concerned family or friends, a more thoughtful decision could be reached for each person. Recent studies indicate that the vast majority of outpatients would welcome the opportunity. Few express anxiety about the topic, and most expect their physicians to initiate the discussion. To simplify the process, several proposals have been made to ease the process and to have forms readily understandable by the general public.

Physicians must begin to broach the topic of advance medical directives routinely and at the earliest possible date with each patient. Failure to consider a written advance medical directive may, in some states, result in unpleasant and prolonged court hearings or, worse, the imposition of life-sustaining treatment when it is no longer desired by the patient.

LAWRENCE K. LOO, MD
ZENO L. CHARLES-MARCEL, MD
Loma Linda, California

REFERENCES

Annas GJ: The health care proxy and the living will. N Engl J Med 1991; 324:1210-1213

LaPuma J, Orentlicher D, Moss RJ: Advance directives on admission—Clinical implications and analysis of the Patient Self-Determination Act of 1990. JAMA 1991; 266:402-405

Lo B, Steinbrook R: Beyond the Cruzan case: The US Supreme Court and medical practice. Ann Intern Med 1991; 114:895-901

Omnibus Reconciliation Act of 1990, 4 USC §4206. Congressional Record, October 26, 1990, p 12638

Clinical Use of Erythropoietin

ERYTHROPOIETIN IS the glycoprotein hormone that regulates erythrocyte production. In the kidneys, specialized "oxygen sensors" detect the tissue delivery of oxygen and modulate the production of erythropoietin to maintain an erythrocyte mass that provides optimal oxygen transport for metabolic needs. Normal erythropoietin levels of 10 to 25 units per liter